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Effects of inert gas narcosis on behavior—a critical review

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Fowler B, Ackles KN, Porlier G. Effects of inert gas narcosis on behavior—a critical review. Undersea Biomed Res 1985; 12(4):369–402.—The effects of inert gas narcosis on behavior before unconsciousness are reviewed with particular attention to four issues. The first is whether the qualitative behavioral effects of all inert gases are identical. Evidence is limited but does not contradict an affirmative answer. This is consistent with the unitary hypothesis of narcosis at the physicochemical level. The second issue concerns the relative merits of four approaches to narcosis; (a) the descriptive model, (b) the hierarchical organization hypothesis, (c) the operant paradigm, and (d) the slowed processing model. It is concluded that the latter two are showing some promise. In particular, operant techniques allow more sophisticated measures of narcosis in animals than behavioral end points, such as loss of the righting reflex. The slowed processing model claims that the majority of performance deficits in humans are caused by a single fundamental deficit, slowing of information processing due to decreased arousal. This slowing is usually accompanied by alterations in task strategy. These alterations, in combination with cumulative slowing in working memory, are said to account for the various manifestations of narcosis on complex tasks. The third issue concerns adaptation to narcosis. There is some evidence that adaptation can occur but it is unclear whether the cause is learning specific to narcosis or development of a physiological tolerance. However, adaptation has not always been found and the variables controlling its presence or absence have yet to be identified. The fourth issue concerns the modifying effects of various factors, such as carbon dioxide and anxiety, on narcosis. Methodological and conceptual problems hinder interpretation of the evidence in this area but, contrary to some current views, there appears to be no conclusive evidence that any factor other than ethanol potentiates narcosis. Some implications of these conclusions for diving operations are discussed.

narcosis
inert gases
behavior
performance
human
animal

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A. INTRODUCTION

This review is concerned with the behavioral effects of inert gas narcosis and the application of this information to understanding and possibly lessening its effects on performance during diving operations. The need for a behavioral approach to narcosis was pointed out some time ago (1, 2), and since then sufficient research has accumulated to justify a review of the literature. The primary focus will be on recent findings but, where necessary, earlier papers will be cited to clarify the development of a line of research. For a detailed history of narcosis an earlier review is recommended (3).

The study of narcosis has traditionally been interdisciplinary in nature, and physiological concepts have influenced behavioral analyses. Therefore, it is helpful to orient the reader and define terms within this wider context. In the broadest sense, the term narcosis refers to the reversible depression of function of an organism, and the term anesthesia, although often used interchangeably with narcosis (4), usually implies the special case of in vivo unconsciousness (5). The study of narcosis includes complex behavior in man and animals, behavioral end-points representing the region of unconsciousness, such as loss of the righting reflex (e.g., 6), electrophysiological indices (e.g., 7, 8) and a vast number of in vitro studies where change is measured at the cellular or biochemical level (e.g., 9, 10). The primary focus of this review will be on studies that assess complex behavior.

Narcosis is induced by the inert gases that are a subgroup of the gaseous and volatile anesthetics. Inert gases are defined as exerting their effects without changing their own chemical structure or the primary chemical structure of biological tissue (11). They include the noble gases xenon, krypton, argon, nitrogen, neon, and helium, as well as hydrogen, nitrous oxide, cyclopropane, and ethylene. Argon, nitrogen, and hydrogen must be breathed under progressively higher pressures to induce narcosis whereas, for practical purposes, neon and helium are considered to be nonnarcotic. All the other gases are narcotic to a greater or lesser extent at atmospheric pressure [*see* (12, 13) for more details on relative narcotic potency]. Historically, the interest of the diving community in this area was sparked by the dangers of breathing air at depths beyond 45 m [5.5 atmospheres absolute (ATA)]. It is now acknowledged that this is due to hyperbaric nitrogen and is commonly referred to as nitrogen narcosis or "raptures of the deep" (4).

The low relative narcotic potency of helium has important practical implications. It can be substituted for nitrogen in the breathing mixture to prevent narcosis, although the high pressure nervous syndrome (HPNS), which is clearly evident at 300 m (31 ATA), ultimately becomes life threatening. HPNS is attributed to the effects of pressure per se and is considered to be a phenomenon distinct from narcosis (14, 15). Although it is beyond the scope of this review to deal with HPNS in detail, the relationship between narcosis and pressure is discussed in section E4.

The present review is primarily concerned with the effects of the inert gases on performance in man and animals from just above the threshold of behavioral change to the point where severe impairment is evident before unconsciousness. In fact, the bulk of this work has employed two gases, nitrogen and nitrous oxide. The former is typically breathed as air in a hyperbaric chamber within the range 4–13 ATA and the latter at atmospheric pressure within the range 15–40% nitrous oxide with the balance oxygen.

Four main topics are covered. The first deals with evidence that the inert gases exert identical behavioral effects. By marshalling evidence to support this view, it becomes reasonable to draw on the broadest possible range of studies when considering the next topic, models of narcosis. Here, studies are arranged according to how they illustrate or support the various approaches to the behavioral analysis of narcosis. This topic is central to the review and requires some knowledge of behavioral techniques and theory. Therefore, since this is an interdisciplinary journal, tutorial sections on relevant concepts are provided. Conversely, some appreciation of physicochemical explanations for the effects of the inert gases is necessary to maintain an appropriate context for evaluating behavioral studies. Reference 14 is recommended as an introduction to this topic.

The final two topics are adaptation to narcosis and the modifying effects of various factors, such as drugs or anxiety, on narcosis. Interest in the former topic arises from whether the effects of narcosis can be lessened to some degree through prior exposure. The latter topic has been studied for two reasons. First, to estimate performance decrements likely to be encountered in diving operations where multiple stressors are invariably present and second, as a methodological tool for theoretical investigations.

B. EQUIVALENCY OF QUALITATIVE EFFECTS BETWEEN THE INERT GASES

The qualitative effects of a gas refer to the pattern of behavioral changes that it produces. These changes are usually assessed by a variety of performance tests but also include subjective symptoms. The classic early description of nitrogen narcosis in man as "euphoria, retardment of the higher mental processes and impaired neuromuscular coordination" (16) provides some insight into this pattern, but such descriptions are not precise enough to compare gases and determine whether their effects are identical. This issue is critical because it relates to whether one or more behavioral models are required to explain narcosis and whether experimentation can be carried out with gases such as nitrous oxide and the results generalized to nitrogen narcosis.

There has been relatively little research on qualitative effects in comparison with quantitative effects. The latter refers to the partial pressures of the gases required to produce some specified change. The question of relative narcotic potency has been of intense interest because of the light it may shed on the molecular mechanisms of narcosis (13). The majority of studies dealing with quantitative effects, however, rely on physiological indices or behavioral end points, such as loss of the righting reflex. Consequently, these studies do not address the question of whether behavior before unconsciousness is affected in an identical manner by all the inert gases.

Turning to this question, one might anticipate identical effects in view of the hypothesis of unitary anesthetic action at the physicochemical level. This hypothesis assumes that all the inert gases act through a common mechanism [*see* (7, 8, 13, 14) for details]. In fact, the available evidence is consistent with a view of qualitative equivalency of behavioral effects. With respect to the noble gases there are two studies, both involving argon and nitrogen, where direct comparisons have been made. One assessed operant responding with rhesus monkeys (17) and the other mental arithmetic and subjective symptoms with trained divers (18). In both studies it was concluded that the two gases could not be distinguished qualitatively. However, there are no comparative studies for the other noble gases although the general consensus is that their effects are identical (12). With respect to other inert gases that are potent at atmospheric pressure, only a few researchers interested in nitrogen narcosis have considered them in the past as substitutes for hyperbaric experimentation (1, 19, 20) despite advantages of experimental simplicity and economy. Perhaps part of this hesitation has been the absence of comparative studies, but it has now been demonstrated that hyperbaric nitrogen and nitrous oxide produce identical effects on components of memory and auditory perception (21, 22) as well as serial choice reaction time (23). It has also been reported that a variety of general anesthetics, including nitrous oxide, cyclopropane, and ethylene, have identical effects on memory (24).

It may be concluded that the qualitative equivalency hypothesis has not been contradicted, although it is quite clear that a much wider range of gases and indices of narcosis must be examined before it can be entertained with other than cautious skepticism. With this proviso in mind, it will be assumed for the present that a unitary behavioral model can account for narcosis and that data for constructing this model can be drawn from appropriate experiments using any inert gas. This course of action is followed in section C.4 without serious contradictions emerging regarding the

effects of diferent gases, although it must be kept in mind that comparisons are primarily restricted to hyperbaric air and nitrous oxide.

C. APPROACHES TO THE ANALYSIS OF NARCOSIS

Four approaches are considered. They are; (a) descriptive model, (b) hierarchical organization hypothesis, (c) the operant paradigm, and (d) slowed processing model.

1. Descriptive model

The roots of this approach lie in the medical-physiological viewpoint which describes narcosis in terms of a set of signs and symptoms. This viewpoint has exerted an important influence on narcosis research for many years (3, 12, 25, 26) although its adequacy as a behavioral model has been questioned (1, 2, 27).

The classic early description of narcosis as "euphoria, retardment of the higher mental processes and impaired neuromuscular coordination" (16) forms the basis for this approach. A modern version of this describes narcosis in terms of its differential effects on three categories of behavior, referred to as cognitive, reaction time, and dexterity, respectively (28). The cognitive category is said to be the most affected by narcosis, and dexterity, the least. With respect to the classic early description, the first two categories represent higher mental processes, and the third neuromuscular coordination. The cognitive category has been defined in terms of sentence comprehension, conceptual reasoning, continuous free association, and mental arithmetic. The reaction time category in terms of one- and two-choice reaction time, digit cancellation, and card sorting, and the dexterity category is represented by the Purdue pegboard and the screwplate test.

The justification for this model is based on collating the results from a number of nitrogen narcosis studies employing these tests and arguing that decrements on the tests cluster as predicted (28). An examination of these data, however, reveals that variability between the categories is sufficiently high to render predictions about individual tests highly unsatisfactory. For example, the data presented in Ref. 28 reveals that decrements on tests in the cognitive category at 4 ATA range from 4 to 34% and this completely encompasses the reaction time category which ranges from about the same lower value to 22%. The cognitive and dexterity categories also overlap by a considerable margin. For different versions of mental arithmetic tests, the decrement at 10 ATA ranges from 15 to 53%. Some of this variation can be attributed to procedural differences between experiments but this is unlikely to be the complete explanation. Therefore, these data indicate that, on the average, cognitive tests are more sensitive than dexterity tests but the model breaks down beyond this point and cannot be regarded as a particularly satisfying explanation for narcosis.

2. Hierarchical organization hypothesis

This model has been used to explain a variety of performance decrements with nitrous oxide (29) and hyperbaric air (30–32) as well as memory loss with a wide range of anesthetics (33). It is derived from Hughling Jackson's notion that the sensitivity of physiological systems to anesthetics depends on their phylogenetic age

(34). Thus, newer, "higher centers" are more sensitive and are affected first. By analogy, it is argued that more "complex" or developed mental functions should be affected by narcosis before less complex functions. The model is assessed by using performance tests that are postulated to tap these mental functions, and it is predicted that the greater the "complexity" of a test the more it will be affected by narcosis.

The difficulty with this model is that the definition of complexity is vague (2, 35). There appears to be no satisfactory way to define degree of complexity except on common sense a priori grounds. Based on this method, predictions from the model are not in accord with the empirical data (29, 36). Generally speaking, it is possible to differentiate between tests in the cognitive and dexterity categories but reliability breaks down beyond this point. Thus, the explanatory power of the model seems to be no better than the descriptive approach to which it bears an affinity.

3. Operant paradigm

This line of research was initiated because of dissatisfaction with behavioral end points as a measure of narcosis in animals (37). In fact, describing the operant paradigm as a model is somewhat of a misnomer because it has been primarily used as a measurement technique. It has, however, evolved into a method which has addressed a number of substantive issues including adaptation and drug interactions. Studies concerned with these issues will be reviewed in later sections. The focus here is on research concerned with the validity and meaning of the operant technique as a means for measuring narcosis.

a. Basic concepts of the operant paradigm

In a typical narcosis experiment a food-deprived animal (usually a rat) presses a bar to receive a pellet of food. The pellet of food is called a reinforcer which modifies the rate of bar pressing, the dependent measure. Bar pressing is maintained by a schedule of reinforcement which specifies the contingent relationship between the responses and the reinforcement. Different schedules of reinforcement can be chosen to produce different patterns of responding. Reinforcement can be continuous or intermittent. In the former case a reinforcement is received for every response. In the latter case reinforcement is contingent on either the number of responses emitted (a ratio schedule) or a time interval (an interval schedule) and both these schedules can be either fixed or variable. This arrangement results in four basic schedules: fixed interval (FI), variable interval (VI), fixed ratio (FR), and variable ratio (VR). For example, with an FI 90 schedule, a reinforcement is provided on the first response that occurs 90 s after the last reinforcement. A VR 30 schedule is one where the number of responses required to obtain a reinforcement will vary in a specified manner around an average of 30.

Three other kinds of schedules have been used in narcosis research. The most popular one has been the differential reinforcement of low rates (DRL) schedule where a response must be withheld for a specified period of time. This schedule can have a limited hold (LH) option so that a response must also be made within specified time limits. For example, DRL 18 LH 6 means a response must occur between 18 and 24 s after the last response for a reinforcement to be delivered. In contrast to the other schedules discussed, a DRL schedule produces low rates of responding and

the addition of the LH option sharpens the time discrimination required to obtain reinforcement.

The second schedule is known as random ratio because only the probability of reinforcement/response is specified so that a reinforcement is received after an irregular number of responses that are not prespecified. Finally, a progressive ratio schedule is one where the number of responses required to obtain a reinforcement increases by a specified number each time reinforcement is delivered until responding ceases within a specified time period. With this schedule, the size of the final ratio achieved, the number of responses completed, or the amount of reinforcement received can be used as dependent measures. More details on the operant technique and its application to the analysis of drugs can be found elsewhere (38–40).

b. Application to narcosis

The first study of narcosis with operant techniques was conducted with rhesus monkeys. The animals were required to perform on a random ratio schedule involving the discrimination of a flashing light while breathing 80% argon or nitrogen and 20% oxygen at 4, 7, and 10 ATA (17). There was a clear decrease in the response rate. This effect was greater with argon than with nitrogen at 10 ATA, but at lesser pressures the two gases could not be discriminated. It was concluded that the response rate was a reliable measure of narcosis and reflected psychomotor decrements analogous to those found with humans.

A more comprehensive study (37) with rats breathing air at 7 ATA examined three schedules, FR 55, DRL 18 LH 6 as well as a multiple schedule comprising alternate FR 20 and DRL 18 LH 6 sequences. Response rate decreased on the FR schedules and increased on the DRL schedules. The latter result signifies a drop in efficiency because more responses are occurring before the time window in which reinforcements can be obtained. It was concluded that both these changes were a manifestation of narcosis with the suggestion that the decreased rate on the FR schedule reflected more than a loss of motor coordination or a decrease in activity level. A different picture of the changes under narcosis on an FR schedule were found in another study using a more sophisticated experimental design and larger groups of rats breathing air at 7, 10, and 13 ATA with two schedules, FR 30 and DRL 15 (41). On the FR 30 schedule, average response rate for the session decreased because time spent responding was reduced at 13 ATA whereas the rate during periods of responding was unaffected. This result obviously has quite different implications compared to one where rate during responding is decreased. On the other hand, the DRL results were more in agreement with the previous work (37), although a difference was first detected at 13 ATA rather than 7 ATA. It was proposed that the increased rate on this schedule was due to a disruption of timekeeping to which others have agreed (42).

By using helium as a control at 7.1 and 8.6 ATA with rats, it has been demonstrated that the increased rate with the DRL 18 LH 6 schedule is due to narcosis and not to other confounding variables in the hyperbaric environment (43). Response rate was broken down into a frequency distribution of interresponse times (IRTs) and there was a shift away from the peak around 18 s toward shorter IRTs with air, while helium had relatively little effect on the distribution. Neon was also investigated in this study. It tended to decrease the number of responses without changing the shape of the distribution. Helium has also been used as a control with pigeons performing

under a multiple FR 30, FI 180 schedule at 2, 4, 7, and 10 ATA (44). There was a clear suppression of response rate with both air and helium and the two mixtures could only be discriminated at 10 ATA, indicating the birds were sensitive to the hyperbaric environment. These results clearly demonstrate the importance of appropriate controls with this methodology.

The sensitivity of various schedules has been investigated using rats performing on VR 50 and DRL 20 schedules at 7.1, 10.2, and 13.3 ATA with air (45). A decrease in both rate and time spent responding on the VR 50 schedule was detected at 10.2 ATA in contrast to 13 ATA for an FR 30 schedule used previously (41). No mention was made of whether rate during responding remained constant. Rate on the DRL 20 schedule was increased at 10.2 ATA but not at 7 ATA, as found previously (37, 43). This difference was thought to be due to either the LH option providing additional sensitivity or different strains of rat.

Rats have been tested on a progressive ratio schedule over a range from 4 to 10 ATA with air (46). It was found that the number of responses completed on the final ratio increased at 4 ATA and then progressively decreased at higher pressures, an effect not evident with the helium control. The effect at 4 ATA was attributed to a decrease in the aversiveness of the large ratios generated at the lower pressure. It is tempting to speculate that this may be related to the euphoria reported by humans under the influence of narcosis. These results also imply that the sensitivity of rats to narcosis may be similar to that of humans because 4 ATA is generally accepted as the lower limit of pressure for detecting nitrogen narcosis (12).

c. Discussion

Three conclusions emerge from these studies. First, narcosis before unconsciousness can be assessed in animals with operant techniques. In this regard, the DRL schedule with the LH option appears to be particularly useful. Although this schedule may not be as sensitive as the progressive ratio schedule, it is probably more practical to implement because it allows sampling of behavior over reasonably short time intervals. With regard to the FR schedule, it is not clear at present whether the changes that have been observed with it reflect a graded decrease in response rate or a decrease in time spent responding. Answers to these questions can be obtained by paying more attention to specifying the form of the changes due to narcosis in a fine-grained manner. This approach is demonstrated by the use of IRT distributions with the DRL schedule. Evidence also suggests that the effects of narcosis could be easily confounded with other stressors in the environment and therefore helium as a control should always be seriously considered. Moreover, although the evidence is slim, rats may be better subjects than pigeons because the latter appear sensitive to the hyperbaric environment (44).

Second, there is reason to think that results with this technique can be generalized to human behavior. Both the range of pressures over which narcosis can be detected and the kinds of deficits that have been observed are consistent with the concept of narcosis based on human studies. Where safety is a consideration with humans, operant techniques could play a valuable role.

Finally, the emphasis to this point has been on demonstrating that narcosis can be measured with operant techniques. A number of hypotheses have been advanced to account for the changes observed with the various schedules, but evidence is lacking

to confirm or deny them. It seems clear that the time is ripe to begin focusing on these more fundamental questions.

4. Slowed processing model

The slowed processing model (23, 47, 48) is based on the information processing approach to the analysis of skilled performance (49) which influenced workers using nitrous oxide in the 1960s (50) but was not applied to nitrogen narcosis until later (2, 51, 52). This model has evolved as a result of the inadequacies of either the descriptive approach or the hierarchical organization hypothesis in explaining the effects of narcosis on human performance.

a. Basic concepts of the information processing approach

Performance is explained in terms of an information processing system, a simplified version of which is illustrated in Fig. 1. This system has three main features. The first is a series of stages, each of which take time to process information (53). These stages are referred to as *structural* variables and are named after the kind of processing they perform, e.g., there are perceptual, stimulus-response, and effector stages (54). Other kinds of structural variables are memory stores which hold information either temporarily or permanently (55).

The second feature of the system is that its overall efficiency is said to be determined by the level of arousal or activation—this is called a *functional* variable (54). Up to a point, increases in arousal improve performance and vice versa (56). The regulatory mechanisms of arousal are not well understood but are currently thought of as being multidimensional in their influence on behavior (57, 58). Within this system, an important role is assigned to the ascending reticular activating system in regulating cortical excitability. The third feature, encompassing *strategic* variables (59), consists of control processes which organize the resources of the system to accomplish a particular task. These processes give the system its complex dynamic characteristics and may or may not be under the conscious control of the performer. They include the distribution of attention, decision criteria, rehearsal strategies, and speed-accuracy trade-off settings. For example, the latter are governed by a speed-accuracy

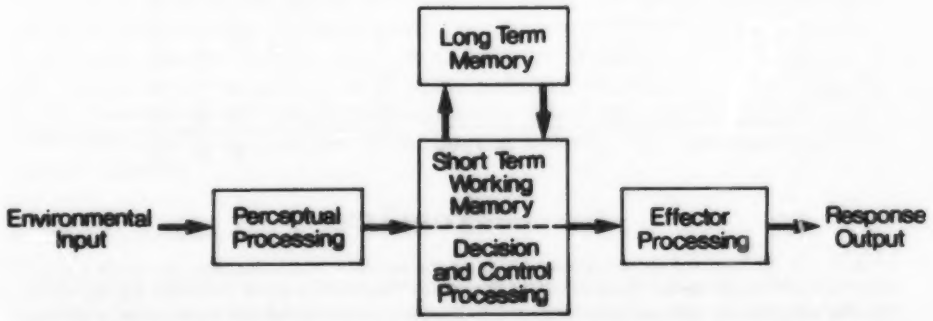

Fig. 1. A simplified version of the stages involved in the information processing system. Each stage takes time to process information and adds an increment to the total time required for a response.

operating characteristic which is illustrated in Fig. 2*A* (60). Performers must strike a balance between speed and accuracy and this speed-accuracy setting, which is influenced by a variety of factors, can have an important bearing on the character of ongoing performance (61).

In terms of the information processing model, narcotic performance deficits, reflected by decreases in the speed or accuracy of responding, could be due to the disruption of structural, functional, or strategic variables, either alone or in combination. Thus, the problem is to partial out the effects of narcosis on each of these features of the system.

The additive factor method (AFM) has been used to isolate the effects of narcosis on the speed of processing of stages. This method assumes that the serial operation of each stage is independent of the other stages such that total reaction time is the sum of times taken by each stage (62). This is illustrated in Fig. 3. When adapted to the study of narcosis, a reaction time task is varied along an appropriate dimension to influence the processing time of the stage under investigation. For example, to assess the effects of narcosis on a perceptual processing stage related to stimulus intensity, reaction time to stimuli of both high and low intensity could be measured. The slope of the reaction time function represents the processing rate of the stage under investigation whereas the intercept represents processing time for the remainder of the stages involved in the task. Therefore, if narcosis increases the slope of the function (an interactive effect) it is assumed that the stimulus-intensity stage is slowed. On the other hand, if the intercept is increased (an additive effect), it is

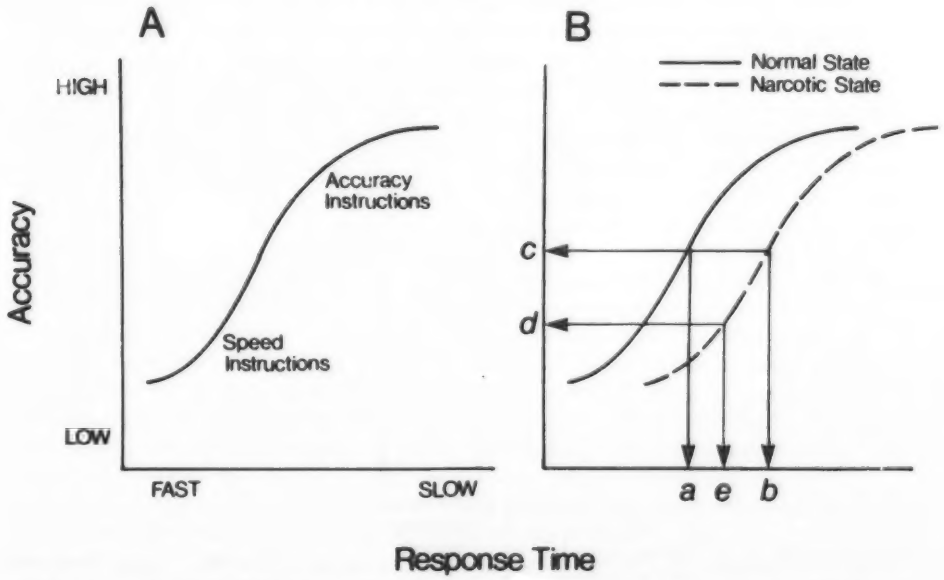

Fig. 2. *A:* An idealized speed-accuracy operating characteristic which illustrates that performance is a balance between the speed and accuracy of responding. Instructions to the performer are one way to shift the setting on the operating characteristic. *B:* Narcosis is assumed to shift the function to the right so that speed decreases from *a* to *b* if accuracy is held constant at *c*. If accuracy is allowed to decrease to *d*, speed only decreases to *e*.

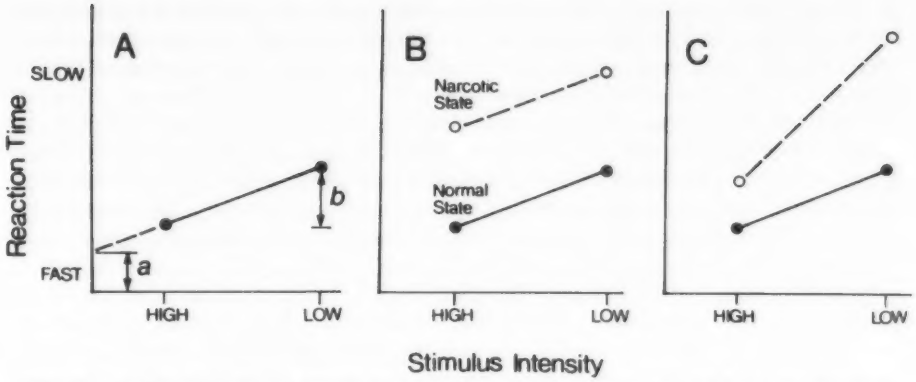

Fig. 3. *A:* The relationship between reaction time and stimulus intensity where *a*, the intercept, represents the sum of times from all stages in the reaction process other than that due to stimulus intensity and *b*, the slope, represents the rate of processing of the stimulus intensity stage. *B:* Narcosis is additive and a constant has been added to reaction time. According to the Additive Factor Method the inference would be that the stimulus intensity stage is unaffected by narcosis. *C:* Narcosis interacts with stimulus intensity and increases the slope of the function while the intercept is unchanged. Inference would be that the stimulus intensity stage is slowed by narcosis.

assumed that some other stage involved in the task is slowed. Of course, the foregoing conclusions only hold when the speed-accuracy setting has been held constant. A potentially serious problem is that the assumptions underlying the method are controversial (60, 62). Therefore, interpretation of data in terms of AFM logic must be made with extreme caution. Nevertheless, it can be argued that the method is useful if it is used in conjunction with other methodologies and an interpretation emerges that is logical from a number of points of view (63).

Signal detection theory (SDT) is another method for distinguishing between the effects of narcosis on structural and strategic variables in threshold perception experiments where fast responses are not required and accuracy is the dependent measure (64). SDT separates the sensitivity of the perceptual system (designated d') from the decision criterion (designated β), the latter being an index of the willingness of the performer to report a stimulus. For example, if a series of trials are given with a barely detectable stimulus randomly presented on half of them, accuracy of detection will depend on both perceptual sensitivity and the relative importance attached to failing to report a stimulus that is actually present (miss), as well as reporting a nonexistent stimulus (false alarm). Thus, accuracy of detection would increase if false alarms are not of great concern to the performer and decrease if they are. The need to disentangle perceptual sensitivity and response bias is of particular concern in narcosis experiments because of the possible influence of subjective sensations, such as euphoria.

b. Application to narcosis

Inferences about the effects of narcosis on structural, functional, and strategic variables have been based on a number of different experimental paradigms which are reviewed below.

i. Speed of processing. It is well known that narcosis increases reaction time and in those studies that can be interpreted in terms of AFM logic a pattern of additive rather than interactive effects emerges. Additivity has been found for stimulus brightness with 35% nitrous oxide (23, Experiment 2), stimulus size with air up to 7 ATA (65), number of stimulus-response choices with up to 35% nitrous oxide (50, Experiment 2) as well as for short-term memory (STM) set size with the general anesthetic enflurane (66). These results have been used to infer that the slowing due to narcosis is not caused by the disruption of processing stages, i.e. it is not a structural deficiency. Rather, it is best accounted for by a decrease in the efficiency of the system as a whole, i.e. a functional change (23, 47).

Recently, more direct evidence that the slowing due to narcosis is a functional effect has come from a study showing that the additive effects of 20% nitrous oxide on a number of stimulus-response choices was exacerbated by alcohol, a central nervous system (CNS) depressant, and ameliorated by amphetamine, a CNS excitant (48). It was concluded that these results are consistent with the idea that narcosis decreases the level of arousal or activation in the CNS and it is this decrease that increases reaction time.

The results from experiments involving the effects of exercise on narcosis also lend some support to the arousal hypothesis. Exercise was originally investigated because it may increase the build-up of carbon dioxide (hypercapnia)—a potential problem in diving operations, particularly if the breathing apparatus causes resistance. In the two experiments discussed below, subjects pedaled a bicycle ergometer while breathing through a mouthpiece and demand regulator, but the resistance of the system was not determined. In the first experiment a workload of 300 kg per m/min was used and manual dexterity and mental arithmetic were assessed at 4, 7, and 10 ATA with air (25, 67). Manual dexterity deteriorated with exercise but there was no significant decrement in mental arithmetic performance. The effect on dexterity was attributed to hypercapnia although carbon dioxide levels were not monitored. Since mental arithmetic was unaffected a more likely explanation is that exercise disturbed dexterity directly (35). It is noteworthy that mental arithmetic showed a trend for improvement with exercise at 4 and 7 ATA and it was speculated that exercise served to "stimulate wakefulness" and counteract the effects of narcosis (67). This possibility is given some support by the results of another study where it was found that progressively heavier exercise (400 and 800 kg per m/min) ameliorated the effects of up to 30% nitrous oxide on a choice reaction time task, but the amelioration was less clear for simple reaction time (68). Hypercapnia was not a factor in this experiment because alveolar carbon dioxide pressure ($P_{A_{CO_2}}$) was monitored and the subjects tended toward hypocapnia.

It would be unwise to draw any conclusions from these experiments concerning the role of exercise in producing hypercapnia during diving operations but they point toward the possibility that, all other factors being equal, exercise may ameliorate narcosis. This hypothesis is consistent with the view that exercise increases level of arousal and performance (69) and thereby counteracts the decrease in arousal due to narcosis.

In summary, the hypothesis that slowing due to narcosis is a functional rather than a structural deficit is a strong one and must be treated with caution on the basis of the present evidence. Some causes for concern are that not all the experiments interpreted in terms of AFM logic may have had the requisite degree of sensitivity to

differentiate between additive and interactive effects. In addition, the number of stages that have been examined is limited. Another question is the ambiguity in the model of how arousal influences slowing. In particular, according to AFM logic, assigning arousal as the cause of the pattern of additive effects implies that it is a stage before those normally discussed in relation to information processing (62). These latter stages are not slowed directly, otherwise a pattern of interactive effects should have been observed in the experiments discussed earlier (23, Experiment 2; 50, Experiment 2; 65, 66). This reasoning leads to the concept of narcosis decreasing arousal and gating information before stage processing—a possibility that is consistent with evidence that visuomotor performance depends on the level of neuronal activity in the reticular system (70, 71). On the other hand, observations from studies of neuronal activity under anesthesia are not in full accord with the early concept of anesthesia as a selective depression of the reticular system (72). Thus, although it seems necessary to invoke the concept of arousal to explain the pattern of behavioral observations discussed above, this concept is not easy to define clearly (73) and the physiological correlates of behavioral slowing remain to be elucidated (7).

ii. Accuracy of processing. Experiments in this area can be broken down into three different categories according to the nature of the experimental paradigm.

The first category involves reaction time or movement time experiments where an increase in error rate often accompanies increased response time. The question arises whether this increased error rate reflects a structural deficit, in the form of a distortion in information transmission, or a shift in the speed-accuracy trade-off setting (a strategic change). If the latter is true, it ought to be possible to either control or manipulate accuracy. An increased error rate under narcosis has been found with a serial choice response time task when accuracy was uncontrolled (23) but not when the subjects were suitably trained (48). Manipulation of speed and accuracy has been demonstrated with a reciprocal tapping task where decreases in both speed and accuracy were found in unrestrained subjects breathing 35% nitrous oxide. However, with training and knowledge of results, accuracy was controlled and it was concluded that this reflected a shift in the speed-accuracy setting (74). These results support the hypothesis that decreases in accuracy are due to a strategic rather than a structural change, at least with this paradigm, but more conclusive evidence is required. This would involve determining the effect of narcosis on a complete speed-accuracy trade-off function. The hypothesized relationship is depicted in Fig. 2*B*.

Two reasons have been proposed for the decreases in accuracy seen with the paradigm discussed above. First, performers prefer to distribute the impact of narcosis between speed and accuracy so that the loss in speed is not as noticeable (*see* Fig. 2*B*). Second, the euphoria induced by narcosis makes the performer less reluctant to maintain a particular setting (74). Thus, to fully understand the effects of narcosis on performance the role of subjective effects must be understood. These will be considered in more detail in a later section.

The second category of paradigm involves perception experiments where speed of processing is not a factor because responses are unpaced and accuracy is the dependent measure. In this type of experiment, a decrease in accuracy could imply a structural disruption of perception or a criterion shift in willingness to report a stimulus.

It has been shown that 30% nitrous oxide has no effect on a variety of simple visual tests, including acuity, stereopsis, optokinetic nystagmus, and accommodation (20). An early report (75) claimed that the judgment of size at a distance is affected by nitrous oxide but this result is questionable. In this experiment three separate groups of subjects breathed either air or 30 or 40% nitrous oxide. The task was to adjust a line within arms reach so that it was equal to a standard line 5.5 m distant that was either 114 or 152 mm long. It was found that nitrous oxide caused the near line to be set longer, implying that the standard was perceived as longer and/or further away. However, a replication of this experiment, except that there was only one narcosis group breathing 35% nitrous oxide, failed to show any effect on accuracy as illustrated in Fig. 4 (Hamilton and Fowler, unpublished experiment). A possible explanation for these contrasting results is that the subjects in the replication were experienced with narcosis and trained to ignore subjective sensations that might influence response bias.

Another report of visual disturbance noted a variety of bizarre effects, such as hallucinations, at 13 ATA with air, although they disappeared rapidly (25). These results are difficult to interpret, both because this dose is approaching the limits of

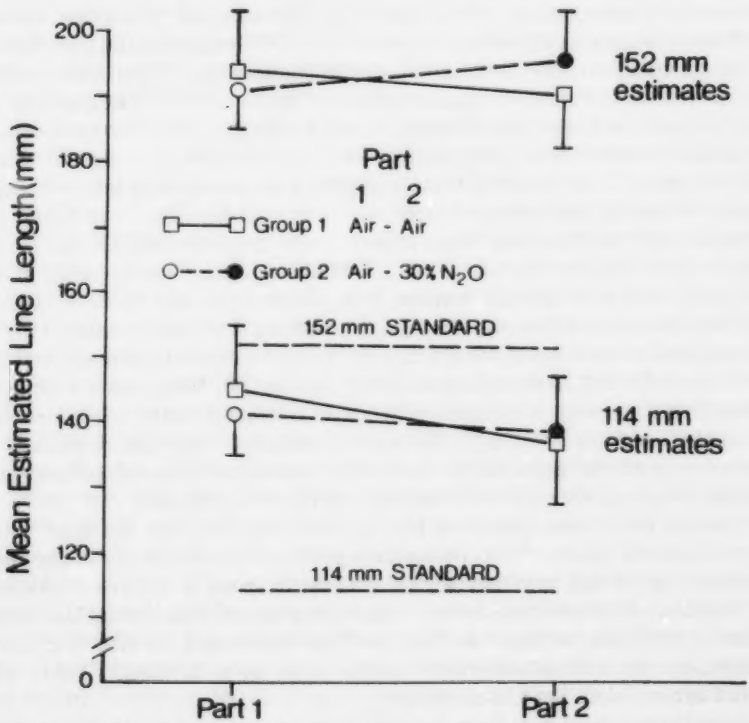

Fig. 4. Effects of nitrous oxide on the judgment of line length. There were two successive parts to the experiment and in each part each subject judged both the 114- and 152-mm standards four times. There were 8 subjects in each group. Group 1 breathed air in both parts and Group 2 breathed air followed by nitrous oxide. Both standards were overestimated but nitrous oxide had no significant effect on judgment. *Bars* represent SEMs.

consciousness and because the rapid adaptation raises the question of whether psychological factors, such as anxiety, were involved.

Regarding auditory perception, raised air conduction but not bone conduction thresholds have been found with air up to 11 ATA (76). This implies impaired sound transmission through the middle ear, perhaps due to a failure to maintain precise equilibration of middle ear pressure with chamber pressure. It has also been found that air conduction word recognition is degraded up to 11 ATA with air (77). This was interpreted as a central perceptual deficit due to narcosis. This conclusion has been questioned because a bone conduction control was not used and it was demonstrated experimentally that digit recognition was degraded by 35% nitrous oxide only when disturbances of sound transmission in the middle ear were not controlled (22). This implies a peripheral, not a central, disturbance.

The argument that narcosis does not affect central auditory perception received additional support from an experiment using 35% nitrous oxide where subjects were required to detect, and later name, a target word buried in a list of words presented to one ear while distracting words were presented to the other ear. It was found that accuracy of detection was unaffected in these circumstances (47). The need for appropriate controls with auditory discrimination experiments in the hyperbaric environment is further demonstrated by the finding that the performance of rats on an auditory discrimination task was impaired to an equal extent by both air and a helium-oxygen mixture up to 8.5 ATA (78).

The accuracy of hand positioning using combinations of two modalities, vision and proprioception, has been examined with up to 30% nitrous oxide (79). Constant error was relatively unaffected for either modality alone but it deteriorated when they had to be matched. The involvement of the somesthetic senses in performance decrements may also be indicated by the finding that body sway is increased by hyperbaric air (80) and nitrous oxide (81). It is well known that narcosis has analgesic effects and this has been demonstrated using SDT where shifts in both d' and β were detected with 33% nitrous oxide (82). The change in β indicated a decreased willingness to report pain. This shows the need to take into account response bias when the effects of narcosis on perception are being analyzed.

The accuracy of time perception is altered by narcosis. Time is judged to pass more quickly with nitrous oxide (83), hyperbaric air (42), and various general anesthetics (84), an effect that has been attributed to the slowing of an "internal clock" (85).

In summary, conclusions from these perception experiments must be made cautiously because the data are fragmentary and there is too often a lack of experimental control over important variables. Obviously, narcosis decreases pain sensitivity and possibly affects other somesthetic senses that could influence complex performance in important ways. The weight of evidence suggests that the accuracy of either vision or audition is unaffected by narcosis, but more definitive experiments are required. The distortion in the accuracy of time perception might be regarded as a structural effect but the hypothesis that it is due to the slowing of an "internal clock" (85) would be quite consistent with a functional slowing of the CNS as discussed in the previous section.

The third category of paradigm involves memory tasks where the dependent variable is accuracy of recall. The effects of narcosis on memory have been of interest because amnesia and learning deficits are important features of narcosis and were

documented by early observers (16, 86). These disturbances might appear to be due to structural deficits, e.g., a decrease in the capacity of a memory store or distortion of information during input or output from a store. This is not necessarily the case. Modern theories of memory emphasize the importance of strategic variables as determinants of recall efficiency with the consequent need to regard memory as a dynamic system (87). In temporary storage and manipulation of information this system has been called working memory and is only partially understood (88, 89).

Tests of STM, which emphasize the assessment of storage capacity in working memory, have been used extensively by narcosis workers. Hyperbaric air and nitrous oxide have no effect on dichotic listening (22, 90) or the digit span (20, 21) and the same holds true with the probe technique for a number of general anesthetics (33). Nitrous oxide does not affect the recency portion of the free recall curve, a measure of storage and/or retrieval efficiency of working memory (22). On the other hand, it has been reported that nitrous oxide reduces the digit span (29). It has been claimed that immediate memory is affected by nitrous oxide (91), but this was based on evidence from a test involving the learning of syllable pairs and therefore reflects long-term memory (LTM). The weight of this evidence leads to the conclusion that the storage efficiency of working memory is largely unaffected by narcosis.

A good deal of interest has centered on LTM as a source of the memory deficits generated by narcosis, and two hypotheses have been proposed. One is that there is a failure to input information into LTM due to some structural deficit (22, 47). This proposal is based on a number of studies using either hyperbaric air or nitrous oxide which demonstrated a learning deficit that was not ameliorated by any of the following manipulations: a return to the normal state (29, 90), word cueing (22), or forced choice recognition (47). An attempt to demonstrate a disruption of memory organization as a cause of learning failure has also been unsuccessful (92). In contrast to these findings, it has been reported that forced choice recognition of material learned while breathing nitrous oxide improved after the event (33). This implies the material had been stored in LTM but was temporarily inaccessible. The developments in memory theory mentioned earlier (87) have led to a second hypothesis that the effects of general anesthetics on memory could be explained by a disruption of the processing required to both encode information into LTM and to retrieve it (24). This hypothesis has been tested without clear-cut success using nitrous oxide in conjunction with the levels of processing paradigm (93, 94). This paradigm is the basis for the theory that the efficiency of memory depends in part on the depth to which information is processed at the time it is presented for learning (87).

The contradictory picture presented above concerning LTM has yet to be resolved. Consequently, there is not at present a compelling explanation for the learning and amnesia effects generated by narcosis. One possible avenue for future research is the role of arousal in narcotic memory deficits since there is evidence to suggest that arousal level can influence LTM (95). An explanation along these lines would provide a parsimonious link to the basic postulate of the slowed processing model.

iii. The role of working memory. It has been postulated that processing occurs in working memory by a series of operations in a manner analogous to the central processing unit in a computer (89). If this is the case, the role of working memory may be critical to understanding the effects of narcosis on complex tasks. If each operation performed in working memory is slowed by narcosis then, due to the

iterative nature of processing, there will be a cumulative slowing and response time will increase as the total number of operations that must be performed to complete the task increases. Evidence supporting the foregoing comes from relatively complex tasks. This complexity can take a number of forms; there may be time constraints in conjunction with the need to store information temporarily or there may be a number of operations that must be executed before arriving at a solution. Mental arithmetic fits into this category, and using the principles outlined above Ref. 23 offers a theoretical analysis of why this task is degraded by narcosis.

Another example of a task involving constraints of time and storage comes from a study where the effects of up to 35% nitrous oxide were examined with the missing scan technique (96, 97). With this technique N-1 items are presented from an ensemble of N items and the missing one must be named. At a fast presentation rate, accuracy was resistant to impairment but response latency increased, whereas at a slow rate the reverse was true. Introspective reports revealed different strategies were used by the subjects depending on presentation rate. At the fast rate all the items were inputted first and then processed by comparison with the ensemble, whereas at the slow rate items were compared with the ensemble at the time of input. Presumably, narcosis affected latency at the fast rate through cumulative slowing generated by the series of time-consuming comparisons made after presentation. On the other hand, slowing was not cumulative at the slow rate and so latency was unaffected. In the case of the fast rate it might be argued that processing capacity was unavailable in working memory to simultaneously deal with incoming items and prevent the ensemble from decaying.

An indication that the number of operations required to complete a task influences the extent to which it is disrupted by narcosis comes from an experiment where 30% nitrous oxide differentially affected four versions of a continuous number coding task (98). From most to least the versions were affected in the following order: adding the previously presented number to the currently presented number, subtracting nine from the current number, adding one to the current number, and naming the current number. A priori, it might be argued that this order corresponds to the amount of processing that must be undertaken to complete each version.

It has also been demonstrated that, when subjects must interpret complex stimuli and keep track of where to respond, nitrous oxide interacts with the number of stimulus-response choices to increase slope as opposed to an additive effect when these processing demands are not present (50). A similar effect has been found at 6.7 ATA with air (99). In Experiment 1 of the latter study, reaction time to various stimulus-response choice combinations was required but the combinations were of low compatibility and had been memorized just before the experiment. It may be that the interactive effect found in this experiment reflects the need to retrieve the freshly learned combinations from LTM.

An interactive effect has also been found between 35% nitrous oxide and target difficulty in a reciprocal tapping task (74). This may be because this task involves the interaction of two processes, ballistic movements and visual feedback required for error corrections (49). Viewing manual dexterity tasks from this perspective also provides an explanation for why they are less sensitive to narcosis than cognitive tasks—dexterity tasks require fewer mental operations compared to cognitive tasks because a proportion of time is spent in ballistic movement which only requires processing at relatively infrequent intervals. Thus there is less opportunity for cumu-

lative slowing which is dependent on the total number of mental operations involved in the task.

In summary, from the point of view of the slowed processing model, it may be possible to analyze even apparently simple tests labeled as "STM" or "mental arithmetic" into a set of operations interacting in a complex manner. Moreover, small changes in the test or the way it is administered may entirely alter the strategy used by the performer for dealing with it. This in turn can alter the manner in which narcosis is manifested in terms of particular combinations of speed and accuracy. These explanations are largely speculative at present because the evidence is indirect. The issue of whether the model can bridge the conceptual gap between slowing as the basic manifestation of narcosis and the translation of this slowing into deficits on complex tasks is an important one and more direct tests of the cumulative slowing hypothesis need to be made.

iv. Subjective effects. Euphoria is a classic symptom of narcosis (16) and the traditional view is that it leads to unreliable behavior, as epitomized by the term "raptures of the deep" (100). Moreover, there are other subjective symptoms and, according to the slowed processing model, the whole constellation of these effects could influence performance in a number of ways. For example, by causing shifts in the values of strategic variables (lack of caution may mean accuracy is allowed to deteriorate) by distracting attention and possibly by creating anxiety, which in turn can degrade performance (101). Inexperience with narcosis might be expected to increase the probability that subjective symptoms influence performance.

The subjective symptoms of narcosis have been examined in detail for hyperbaric air and argon-oxygen (18) as well as for nitrous oxide up to 35% (91). The former study used an adjective check list and identified four clusters of adjectives related to euphoria (e.g., more carefree and cheerful), state of consciousness (e.g., more fuzzy and hazy), work capability (e.g., less effective and efficient), and inhibitory state (e.g., less cautious and self-controlled). Both studies used rating scales and demonstrated that the magnitude of the subjective effects of narcosis could be reliably related to dose level by the subjects. Further, in one of the studies (18) it was suggested that performance feedback modified the subjective estimates of narcosis.

It is somewhat surprising that so few studies have examined subjective effects despite wide acknowledgment of the influence that they may have on performance. The present evidence leads to the following conclusions. First, there is a cluster of symptoms that describe narcosis. Consequently, use of the single term "euphoria" is at best incomplete and possibly misleading. It may be that other symptoms have as much or more influence on performance. Second, the narcotic individual can reliably identify these symptoms. If this fact is taken together with earlier evidence that speed-accuracy trade-off settings can be controlled with training (48, 74), then disorganized behavior may not be a necessary concomitant of narcosis. This has important practical implications. It may be that divers can be trained to monitor their own subjective symptoms, either to prevent the occurrence of life-threatening situations (102) or to control more subtle disturbances in skilled performance, such as shifts in speed-accuracy settings.

c. Discussion

To summarize, the slowed processing model explains narcosis by a single underlying functional effect—slowing due to decreased arousal. This is manifested by an

increase in response time and, often, by a decrease in accuracy. The latter is assumed to reflect strategic rather than structural factors and is not regarded as a necessary concomitant of narcosis. To understand how narcosis disrupts relatively complex tasks, it is necessary to consider the information processing system as being dynamic and involving such factors as cumulative slowing in working memory and alterations in strategy, possibly interacting in a complex manner.

It may be concluded that the slowed processing model is proving to be more productive than either the descriptive approach or the hierarchical organization hypothesis because it appears capable of explaining a good deal of data while offering avenues for testing these explanations.

D. ADAPTATION TO NARCOSIS

It was observed from the outset that repeated exposures to narcosis appeared to lessen its effects (86). These observations have become common lore in the diving community (e.g., 103–105) but it is only recently that this question has been examined experimentally.

The first adaptation study (106) repeatedly exposed rats performing on a DRL 16 LH 6 schedule to air at 7.1 ATA. A gradual improvement in performance was found which could not be attributed to either baseline changes in performance or adaptation to the increased noise levels in the chamber. Two possible explanations were offered for these results; either adaptation of the behaviors disrupted by narcosis (narcosis specific learning) or the development of a physiological tolerance. On the other hand, no adaptation was found with rats on VR 50 and DRL 20 schedules at 13.3 ATA with air (45). It was proposed that this may have been due to the relatively long interval of 7 d between exposures, implying a physiological tolerance explanation for the results of the earlier study.

Since these early animal studies the focus has shifted to human subjects. In the first of these experiments an improvement was found on an adaptive tracking task on the second exposure to air at 7 ATA relative to a 2 ATA control (107). It was proposed that this effect could only be accounted for by some factor specific to the narcotic situation and not simply by exposure to the hyperbaric environment. This view is consistent with the finding that the level of narcotic performance decrement is unrelated to amount of diving experience (31, 108). In support of the situation-specific claim, improvement on a serial choice reaction time task with 35% nitrous oxide has been reported over two sessions, 2–7 d apart, with no change in the control conditions (48).

Contrary to the foregoing studies, no evidence of adaptation has been found using choice reaction time and tracking at 7 ATA with air (99). Improvement was noted, but it was proportional for both the control and experimental conditions. A similar effect has been observed in a very comprehensive study with exposure at 1-d intervals to air at 7 ATA using a variety of measures (109). It was concluded that these results cast doubt on the notion of performance adaptation and that the idea had grown up because of either a failure to distinguish learning that was nonspecific to the narcotic state or adaptation of subjective symptoms had been mistaken for performance adaptation. Some evidence in support of the possibility that subjective symptoms adapt comes from a recent study involving a 6-d air saturation dive at 6 ATA (110).

There were indications that subjective ratings of narcosis declined over this period, but because performance tests were unaffected the relationship between the two remains unclear.

The conflicting results reviewed above suggest that any simple generalizations about adaptation are likely to be misleading. Evidence of improvement in performance is difficult to account for except by a factor specific to narcosis (48, 106, 107). It is not clear, however, whether this reflects learning specific to narcosis or the development of a physiological tolerance. The fact that some studies have failed to demonstrate adaptation (99, 109) seems to favor the former explanation, because it is not hard to imagine that some factors, such as degree of previous learning on the task, could differ between studies and thus influence adaptation. In this regard the nature of the task is not a strong candidate since tracking has been used to demonstrate both the presence and absence of adaptation (107, 109). Other important questions arising from the latter study are whether subjective symptoms adapt and whether they can be mistaken for performance adaptation. There is evidence that the level of narcotic performance can influence subjective estimates of narcosis (18), and it is possible that, in the absence of performance feedback, estimates of ability to perform could be based on subjective symptoms, especially in inexperienced divers.

In summary, issues for future research in this area include: (a) confirmation that under some circumstances adaptation occurs with identification of the variables controlling its presence or absence; (b) given adaptation occurs, determining whether it applies to subjective symptoms, objective performance, or both; and (c) determining whether the explanation for adaptation is learning specific to narcosis, development of a physiological tolerance, or both. This latter issue could be resolved by an experiment involving the appropriate manipulation of time intervals in a test-retest procedure inasmuch as a learning explanation implies a relatively permanent change whereas a tolerance explanation does not (111).

From the practical point of view it appears that the broad statements about adaptation to narcosis found in current textbooks are too general and possibly misleading (e.g., 103–105). It is hoped that the fruits of a research program, such as the one outlined above, will eventually provide more accurate and specific advice to the diving community. Such advice need not be limited to specifying the circumstances under which narcotic adaptation occurs. More emphasis should be put on lessening the effects of narcosis through nonspecific learning, a demonstrably useful technique (109, 112). Nonspecific learning may be an important source of variation in hyperbaric air studies conducted at 4 ATA or higher which have either been unable to demonstrate performance decrements or have found rapid adaptation (110, 113, 114). These studies have in common the use of highly practiced subjects and, since a pressure of 4 ATA is commonly held to be the threshold for detecting narcosis (115), the inference can be drawn that it was raised through practice.

E. THE MODIFYING EFFECTS OF VARIOUS FACTORS ON NARCOSIS

It is well understood that performance in the underwater environment is likely to be influenced by a combination of factors such as carbon dioxide, cold, anxiety, reduced visibility, etc. Consequently, from the practical point of view, there has been interest in determining the effects of narcosis in combination with factors that could

be present during diving operations. To a lesser degree this technique has been exploited as a means for gaining insight into the underlying causal mechanisms of narcosis.

The terminology, methodology, and interpretation of how factors act together has been somewhat ambiguous and needs to be clarified. It is possible to specify both the direction and size of the effect of a factor in combination with narcosis as illustrated in Fig. 5. With respect to direction, the term impairment will be used to refer to a factor which, when combined with narcosis, causes a further deterioration in performance beyond that caused by narcosis alone. The term improvement refers to the rarer case of a factor that reverses the effects of narcosis on performance. An example of such a factor is exercise, discussed in section 4b(i). For the size of an effect the standard terms antagonism, addition, and synergism will be used (13). They refer to a combined effect being proportionately less than, equal to, or greater than the sum of the separate effects of narcosis and the factor, respectively. It is important to note that these terms merely describe the direction and size of a performance effect and do not necessarily connote anything about underlying causal mechanisms. Where it is implied that a factor modifies narcosis through a common underlying mechanism, the terms potentiation and amelioration, corresponding to impairment and improvement, respectively, will be used.

1. Carbon dioxide and oxygen

Hypercapnia is an ever-present problem in the underwater environment and its effects in combination with narcosis have always generated a good deal of interest. In fact, it has been proposed that nitrogen narcosis is caused largely by an accumu-

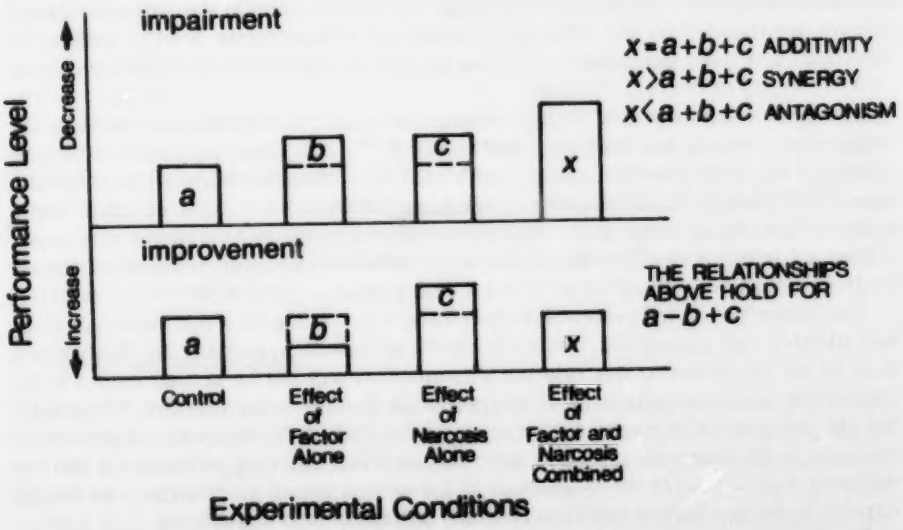

Fig. 5. Possible experimental outcomes which define the effect of a factor on narcosis. In this scheme impairment and improvement are defined by whether the effect of the factor and narcosis combined is bigger or smaller, respectively, than the effect of narcosis alone. The outcome illustrated represents additivity.

lation of carbon dioxide (116) but this theory is no longer considered tenable (117). Oxygen is included in this section because interest in it stems from a link with carbon dioxide—increasing the partial pressure of oxygen can lead to hypercapnia.

Until recently it has been widely held that carbon dioxide potentiates narcosis, a claim stemming from the apparent finding that this gas acts synergistically with narcosis (118). Later evidence cited in support of this view came from a study where it was found that increasing the partial pressure of oxygen when the partial pressure of nitrogen was held at 4.9 ATA led to a synergistic impairment in reaction time and mirror drawing (119). It was proposed that oxygen potentiated the effects of narcosis indirectly by interfering with the elimination of carbon dioxide. A synergistic effect of oxygen with hyperbaric nitrogen has been reported using rats performing on a DRL 18 LH 6 schedule, although 2 of the 3 rats also showed synergy with helium at the highest partial pressure of oxygen (120). The same protocol has been used with an FI schedule but the results of this study are difficult to interpret because an unusual inverted-U dose-response function was found for narcosis (121).

More recently the relationship between carbon dioxide and narcosis has been assessed directly by varying the partial pressure of the former gas with air at 6 ATA while holding oxygen partial pressure constant (122). A tracking task and the Stroop test (reaction time to a stimulus that produces conflict) were used and alveolar carbon dioxide pressure ($P_{A_{CO_2}}$) was measured. For both tests additivity, not synergy, was found. It was concluded that synergy was an artifact arising from the measurement of inspired carbon dixoide rather than $P_{A_{CO_2}}$. In a further study, $P_{A_{CO_2}}$ was found to be additive with air at 8 ATA for mental arithmetic, but while carbon dioxide degraded manual dexterity, hyperbaric air did not (32). In the same study oxygen partial pressure was also varied independently at 1.7 ATA and found to parallel the pattern of effects found for hyperbaric air. This pattern, along with the size of performance effects as predicted by the lipid solubility theory of anesthesia, led the authors to conclude that the mechanism underlying carbon dioxide narcosis is different from that of oxygen or nitrogen narcosis.

It has been demonstrated that, in contrast to cognitive and dexterity tests, body sway shows synergy between $P_{A_{CO_2}}$ and air at 8 ATA (123), an effect greatly enhanced when the eyes are closed. Inasmuch as vision is a powerful source of cues for the control of balance, the enhanced synergy when these cues are removed could imply a deficit specific to some other part of the balance system. Alternatively, it might reflect a confounding effect due to the hyperbaric environment, because increased body sway has been observed at 13 ATA with helium-oxygen (124).

The somewhat limited evidence reviewed above favors the view that carbon dioxide has additive, not synergistic, effects in combination with hyperbaric air. Body sway may be an exception to this rule but this question will not be settled until a body sway experiment is conducted with an appropriate helium-oxygen control. The crucial but slender piece of evidence, which suggests that carbon dioxide does not potentiate narcosis, is the demonstration that these factors affect different performance tests in different ways (32). On the hypothesis of a common causal mechanism, one would expect to see two factors exhibit a common pattern of intertest effects.

The foregoing work also suggests that more attention should be paid to the effects of hypercapnia on performance during diving operations. Decrements in performance have been demonstrated to occur above a $P_{A_{CO_2}}$ of 53 mbar (32) and yet it is known that a $P_{A_{CO_2}}$ of 67 mbar and above is not uncommon in trained divers who hypoven-

tilate (125). Dizziness is a symptom common to both narcosis and hypercapnia and the interesting question arises of whether even experienced divers mistake the subjective symptoms of hypercapnia for narcosis. In principle, it should be possible to discriminate between them, at least with relatively severe doses, because the headache and nausea of hypercapnia differ from the euphoria of narcosis.

The evidence concerning the effects of hyperbaric oxygen on performance and its relationship to narcosis is too contradictory to draw any conclusions at the present time. It has been claimed that hyperbaric oxygen parallels the effects produced by hyperbaric air (32), but an earlier study failed to find any effect of oxygen at 3 ATA on reaction time (126). Other evidence against an intimate relationship between nitrogen narcosis and oxygen narcosis comes from a study using the operant technique with rats (127). The reinforcer was electrical self-stimulation of the brain on a continuous schedule. Rate of responding decreased up to 10.1 ATA with air, but when the partial pressures of oxygen and nitrogen were manipulated independently response rate only decreased with increasing partial pressures of oxygen.

2. Miscellaneous drugs

In an earlier review on drugs and diving, the paucity of studies on narcosis was noted (128). Since then, interest in the area has increased. In particular, a number of studies have appeared which have used ethanol and amphetamine and which have theoretical implications concerning the nature of narcosis. In this section, recent studies with other drugs will be reviewed briefly and then ethanol and amphetamine will be dealt with more fully in section 3.

It has been claimed that naloxone ameliorates narcosis, with the implication that opioid receptors are involved in its mechanism of action (129, 130), but subsequent investigations have not supported this finding (131–133). The latter study also found that physostigmine did not ameliorate narcosis, whereas it has been reported that lithium chloride does (134).

The foregoing studies relied on behavioral end points in animals but operant techniques have also been used. It has been found that Δ^9-tetrahydrocannabinol increases response rate on a DRL schedule but when combined with hyperbaric air, response rate is reduced. This was interpreted as an amelioration of the effects of Δ^9-tetrahydrocannabinol (135). On the other hand, the same drug was reported to prolong unconsciousness induced by a variety of anesthetic agents in mice. This was interpreted as potentiation (136).

3. Ethanol and amphetamine

Ethanol is considered to depress the CNS and amphetamine to excite it, at least over certain dose ranges (137, 138). It has generally been accepted that over a major part of the dose range, narcosis depresses the CNS. Therefore, ethanol should potentiate narcosis and amphetamine should ameliorate it. However, it has been claimed that these drugs have precisely the opposite effects and consequently the conception of narcosis as a CNS depressant may be in need of revision (139).

The claim that ethanol ameliorates narcosis is contradicted by a number of recent studies which indicate the opposite. Ethanol prolonged unconsciousness in mice when combined with hyperbaric air (140). In man, it synergistically impaired body

sway with air up to 7 ATA (141) and caused additive impairment with 35% nitrous oxide for serial choice reaction time (48). It should be noted that the synergistic effect for body sway parallels the carbon dioxide data reviewed earlier. Again the issue is, what mechanisms are being assessed by this measure of narcosis?

Turning to amphetamine, the claim that it potentiates narcosis (139) is based on results using a DRL 18 LH 6 schedule with rats (142, 143). Amphetamine alone was found to increase response rate and, when combined with hyperbaric air, the rate increased even more. Since a rate increase on this schedule reflects a deterioration in performance, these results were interpreted as potentiation. On the other hand there are results that support the contrary argument. Amphetamine in combination with hyperbaric air reduced the rate of responding on an FR 20 schedule over that found with amphetamine alone (142). Similarly, amphetamine alone increased the number of reinforcements received with a progressive ratio schedule but air at 7.1 ATA counteracted this increase, except at the lowest doses (144). In man it has been concluded that amphetamine ameliorated the effects of 20% nitrous oxide on serial choice reaction time (48).

The conflicting evidence concerning amphetamine can be resolved if it is noted that the increased rate of responding induced by hyperbaric air on a DRL schedule has been attributed to the disruption of a temporal discrimination (42), whereas the increase with amphetamine can be accounted for by hyperactivity and stereotyped responding (138, 145). From this point of view, the increased rate when hyperbaric air and amphetamine are combined represents the summation of two unrelated mechanisms rather than the potentiation of narcosis. These ambiguities emphasize the need to understand why narcosis alters operant behavior. Without this information, interpreting a particular pattern of impairment or improvement is difficult.

In summary, the weight of evidence favors the conclusion that ethanol exacerbates narcosis and amphetamine ameliorates it. This is consistent with the view that narcosis depresses the CNS.

4. Pressure

The anesthetic effects of a narcotic gas can be reversed by exposure to higher pressures using an additional gas, such as helium, which is relatively nonnarcotic. This pressure-reversal phenomenon has been of great interest because it has implications for theories of general anesthesia at the cell membrane level (14, 146).

The relationship between narcosis and pressure has recently been reviewed in detail (147). An important point to emerge from this review is that the question of whether pressure ameliorates narcosis at the molecular level or by mutual interaction at some higher level is unresolved. The authors note that the practical implications of this for diving operations are that it may be dangerous to prevent performance decrements due to HPNS with a narcotic gas if this masks pathological changes at the cell membrane level.

From the perspective of the present review, it may be noted that the conclusions above are based on studies using physiological subsystems or behavioral end-points as indices of narcosis and HPNS. There are numerous high pressure saturation studies employing humans but their primary focus has been to answer practical questions (15). In these studies, both safety considerations and the use of small groups of subjects hinder ability to design experiments that will contribute to answering some

of the issues raised in Ref. 147. Therefore, an argument can be made for the cost-effectiveness of using operant techniques in this context to allow the manipulation and simultaneous assessment of narcosis and HPNS (148, 149) before unconsciousness. Some evidence pointing to the feasibility of this approach comes from the results of a study where rats ceased responding on an FR 25 schedule at 12.9 ATA of nitrogen but resumed when pressure was increased to 24.2 ATA with the addition of helium (150).

5. Anxiety

The combination of anxiety and narcosis is particularly difficult to study because anxiety cannot be manipulated easily. Consequently, investigators have relied on open-water diving experiments with relatively inexperienced subjects who are likely to become anxious in this environment. These field studies have the advantage of providing realistic estimates of performance decrements likely to be encountered in diving operations. Their disadvantage is the difficulty of disentangling the causes of a decrement due to the variety of factors that are invariably present.

This line of research was initiated when it was found that the decrement with air in a hyperbaric chamber was much greater at an equivalent depth in the open sea, even when the effects of working underwater were taken into account (108). The same thing was demonstrated for both manual dexterity and mental arithmetic at a depth equivalent to 7 ATA when a helium-oxygen control was used (151). Other studies have led to the conclusion that anxiety is implicated in this effect (152–155). The possibility has been raised that anxiety may interact (synergistic impairment) with narcosis (35, 51) but more recently it has been concluded that the present evidence is not sufficiently clear to choose between additivity and synergy (155). The basic problem appears to be the difficulty of manipulating narcosis and anxiety independently of one another so as to meet the criteria illustrated in Fig. 5.

The experiments discussed in this section provide important information about the complexities of predicting the kind and size of decrements likely to be encountered in actual diving operations and they deserve more attention in secondary sources which synthesize this kind of information (e.g., Ref. 28). The question of the relationship between anxiety and narcosis awaits a solution to the problem of measuring and manipulating anxiety in a controlled manner.

6. Discussion

The present evidence points to the exacerbation of narcosis by ethanol and its amelioration by amphetamine. The mechanism underlying these effects appears to be a common one which can be expressed as a dimension of excitation—depression in the CNS. The evidence also favors the view that carbon dioxide does not potentiate narcosis, despite long-held beliefs to the contrary. None of this evidence is particularly strong and more data are obviously required. If these questions, as well as others raised in the preceding sections, are to be settled definitively, then two problems in this general area need to be addressed.

The first is that not all experiments have been designed appropriately to allow a clear determination of the direction and size of an effect as defined in Fig. 5. The second point is that claims about whether a factor potentiates or ameliorates narcosis

are often based on fuzzy criteria. One aspect of the latter problem can be seen with such popular tests as mental arithmetic or manual dexterity. These tasks are relatively complex, in the sense of the number and nature of the information processing mechanisms utilized to complete the task, but they are simple in the sense that only speed and accuracy are used as dependent measures. From this perspective, it becomes apparent that a factor and narcosis in combination could be affecting the same part of the system (a common cause) or different parts (different causes) with no clear means for differentiating between these possibilities on the basis of the dependent measures. This is true whether or not additivity or synergy is found.

Another aspect of the problem is exemplified by the case of ethanol and narcosis. In an earlier section it was concluded that ethanol potentiates narcosis in the sense that both influence a common mechanism—arousal or level of excitation in the CNS. Yet it would probably not be difficult to show differences between ethanol and narcosis using appropriate tests of muscular coordination. Loss of muscular coordination with narcosis is relatively mild (74) and the slurred speech and staggering gait characteristic of ethanol intoxication are absent. One obvious explanation for this is that both narcosis and ethanol affect one part of the information processing system in common (arousal) but have differential effects on another part (effector control).

Three strategies can be usefully employed to deal with this problem. The first is to use a number of relatively complex tests where inferences about underlying mechanisms are drawn from the pattern of intertest results (32). The second is to use relatively simple tests which allow isolation of components of the information processing system with inferences being drawn from the pattern of intratest results (48). The third is to use relatively complex tests which can be decomposed into parts reflecting underlying components of the information processing system (22, 23). Probably these three methods will have to be combined in a systematic manner if the conceptual and methodological pitfalls in this area are to be overcome.

The issues raised above are not just of academic concern. Lack of clarity in the area has probably contributed to some questionable advice being supplied to the diving community. It has been stated that narcosis is potentiated by anxiety, cold, fatigue, motion sickness remedies, sedatives, hard work, carbon dioxide, and ethanol (156–158). On the present evidence it only seems reasonable to make this assertion about ethanol and, as discussed above, it is not necessarily the case that ethanol and narcosis would show an identical pattern of effects across a variety of tasks relevant to diving operations. Thus there is a case for the argument that the ability to provide accurate and useful advice to the diving community is intimately tied to the problem of developing adequate theoretical models of how a factor acts in combination with narcosis.

F. GENERAL DISCUSSION

The overall conclusion arising from this review is that the call for the application of behavioral techniques to the problem of narcosis (1, 2) has been justified. Some general trends and their implications are particularly noteworthy.

First, the hypothesis of qualitative equivalency of behavioral effects between the inert gases deserves more stringent testing in the future. It offers the potential of more parsimonious theorizing, access to a broader data base, and the ability to utilize

more economical and safe procedures for human experimentation by employing gases that are narcotic at the surface. It is important to note that, for the present, a very cautious approach should be taken to implementing any procedures relevant to diving operations based on experimental results from gases such as nitrous oxide. Such results should first be replicated with hyperbaric air. This would preserve safety and simultaneously test the qualitative equivalency hypothesis.

Second, it has been established with operant techniques that narcosis can be assessed in animals before unconsciousness. Thus, these techniques have great potential where human safety is a concern. Given current misgivings over human involvement in very deep saturation dives and the difficulty of designing experiments under these conditions, operant techniques could play a valuable role in allowing complex behavior to be assessed while manipulating both narcosis and pressure in a manner unacceptable with humans. However, any enthusiasm for operant techniques must be tempered by the realization that our knowledge of why changes occur on different schedules is extremely limited. For example, does the decrease in efficiency on a DRL schedule reflect a change in time perception? Does the slowing on an FR schedule represent an overall decrease in activity or a deficit in some particular locus, such as the motor system? These issues should be addressed and solved if the potential of the operant method is to be fully realized.

Third, the information processing approach to performance, as manifested by the slowed processing model, appears to be a productive theoretical framework for the analysis of narcosis in humans. It allows emphasis to be put on the question of why performance breaks down on a test rather than which test best assesses, or is most sensitive to, narcosis. The latter question has proven to be a chimera, as evidenced by the current tests of narcosis that are essentially identical to those used on the first occasion it was measured objectively (86).

The view of narcosis that emerges from this model is that not all performance deficits are a necessary characteristic of narcosis. Deficits that reflect shifts in the values of strategic variables can, in principle, be controlled within limits. Taken in conjunction with the evidence that nonspecific learning can serve to lessen narcotic performance deficits, potentially important practical implications follow. Traditionally, narcosis has been seen as inducing erratic behavior over which the diver has little or no control and this is reflected in current descriptions of narcosis provided for the diving community (26, 156, 157). Consistent with this view is a lack of advice on how to cope with narcosis (100, 104, 156, 158), although there are exceptions to this (105). There is now a case for reassessing this position. Narcosis is dangerous and should be avoided, but in practice this is not always possible. Therefore, current behavioral knowledge should be applied to the question of whether training and indoctrination procedures can be developed that would increase the safety and work effectiveness of divers exposed to narcosis.

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Fowler B, Ackles KN, Porlier G. Effets de la narcose aux gaz inertes sur la comportement—une revue critique. Undersea Biomed Res 1985; 12(4):369–402.—Les effets de la narcose aux gaz inertes sur le comportement, avant la perte de conscience, sont revus avec une attention particulière portée sur 4 points. Le premier consiste à établir si les effets qualitatifs de tous les gaz inertes sur le comportement sont identiques. Les évidences sont peu nombreuses mais

ne contredisent pas la réponse affirmative. Ceci est conforme avec l'hypothèse unitaire de la narcose au niveau physicochimique. Le deuxième point concerne les mérites relatifs de 4 approches pour expliquer la narcose: (a) le modèle descriptif, (b) l'hypothèse d'organisation hiérarchique, (c) le modèle de conditionnement renforcé, et (d) le modèle opérationel ralenti. Il est conclu que les deux dernières montrent certain signes encourageants. En particulier, les techniques opérationnelles permettent plus de mesures sophistiquées de la narcose chez les animaux que les indices terminaux de comportement, comme la perte du réflexe de redressement. Le modèle opérationel ralenti postule que les déficits de performance chez les humains sont causés en majorité par un simple déficit fondamental, un ralentissement dans le traitement de l'information du à une diminution de l'état d'éveil. Ce ralentissement est habituellement accompagné de changements dans la stratégie reliée à la performance d'une tâche. Ces modifications, en combinaison avec le ralentissement cumulatif dans la mémoire opératoire, seraient responsables des diverses manifestations de la narcose dans l'accomplissement des tâches complexes. Le troisième point concerne l'adaptation à la narcose. Certaines évidences indiquent qu'une adaptation peut survenir mais il est incertain si la cause est l'apprentissage spécifique à la narcose ou le dévelopement d'une tolerance physiologique. Cependant, l'adaptation n'a pas toujours été trouvée et les variables contrôlant sa présence ou son absence sont inconnues. Le quatrième point concerne les effets modifiants de divers facteurs sur la narcose, tel que l'anhydride carbonique et l'anxiété. Les problèmes méthodologiques et conceptuels nuisent à l'interpretation des observations dans ce domaine, mais contrairement à certains points de vue, il n'y aurait pas d'évidences concluantes que tous factors autre que l'éthanol potentialisent la narcose. A partir de ces conclusions, certaines implications sont discutées à propos des opérations de plongée.

narcose
gaz inertes
comportement
performance
humain
animal

REFERENCES

1. Jennings RD. A behavioral approach to nitrogen narcosis. Psychol Bull 1968; 69:216–224.
2. Fowler B. Some comments on "A behavioral approach to nitrogen narcosis." Psychol Bull 1972; 78:234–240.
3. Bennett PB. The aetiology of compressed air intoxication and inert gas narcosis. London: Pergamon Press, 1966.
4. Behnke AR. Inert gas narcosis. In: Fenn WA, Rahn H, eds. Handbook of physiology. Respiration. Washington DC: American Physiological Society 1965: Sec 3, Vol 2:1059–1067.
5. Richards CD. Anesthetics and membranes. In: Metcalfe JC, ed. International review of biochemistry. Biochemistry of cell walls and membranes II. Vol. 19. Baltimore: University Park Press, 1978.
6. Brauer RW, Way RO. Relative narcotic potencies of hydrogen, helium, nitrogen and their mixtures. J Appl Physiol 1970; 29:23–31.
7. Fowler B, Ackles KN. Does the evoked response measure inert gas narcosis? Undersea Biomed Res 1977; 4:81–87.
8. Leitch DR, Hallenbeck JM, Greenbaum LJ Jr. The effects of various gases on cortical and spinal somatosensory evoked potentials at pressures up to 10 bar. Aviat Space Environ Med 1983; 54:105–111.
9. Fink BF, ed. Molecular mechanisms of anesthesia I. New York: Raven Press, 1975.
10. Fink BF, ed. Molecular mechanisms of anesthesia II. New York: Raven Press, 1980.
11. Featherstone RM, Muehlbacher CA. The current role of inert gases in the search for anesthesia mechanisms. Pharmacol Rev 1963; 15:97–148.
12. Bennett PB. Nitrogen narcosis. In: Bennett PB, Elliott DH, eds. The physiology and medicine of diving. Third ed. London: Baillière, Tindall, 1982:239–261.
13. Miller JC, Miller KW. Approaches to the mechanisms of action of general anesthetics. In: Blaschko HKF, ed. Physiological and pharmacological biochemistry. London: Butterworth, 1976:39–76.

14. Smith EB. The chemistry of deep-sea diving. Chem Br 1984; July:625–628.
15. Bennett PB. The high pressure nervous syndrome in man. In: Bennett PB, Elliott DH, eds. The physiology and medicine of diving. Third ed. London: Baillière, Tindall, 1982:262–296.
16. Behnke AR, Thomson RM, Motley EP. Psychologic effects from breathing air at four atmospheres pressure. Am J Physiol 1935; 112:554–558.
17. Burns JD. Hyperbaric gas effects on critical flicker frequency in the rhesus monkey. Physiol Behav 1971; 7:151–156.
18. Fowler B, Ackles KN. Narcotic effects in man of breathing 80–20 argon-oxygen and air under hyperbaric conditions. Aerosp Med 1972; 43:1219–1224.
19. Dickson JG, Lambertsen CJ, Cassils JG. Quantitation of performance decrements in narcotized man. In: Lambertsen CJ, ed. Underwater physiology. Proceedings of the fourth symposium on underwater physiology. New York: Academic Press, 1971:449–455.
20. Biersner RJ. Selective performance effects of nitrous oxide. Hum Factors 1972; 14:187–194.
21. Biersner RJ, Hall DA, Neuman TS, Linaweaver PG. Learning rate equivalency of two narcotic gases. J Appl Psychol 1977; 62:747–750.
22. Fowler B, White PL, Wright GR, Ackles KN. Narcotic effects of nitrous oxide and compressed air on memory and auditory perception. Undersea Biomed Res 1980; 7:35–46.
23. Fowler B, Granger S, Ackles KN, Holness DE, Wright GR. The effects of inert gas narcosis on certain aspects of serial response time. Ergonomics 1983; 26:1125–1138.
24. Adam N. Disruptions of memory functions associated with general anesthetics. In: Kihlstrom JF, Evans FJ, eds. Functional disorders of memory. New York: John Wiley & Sons, 1979: 219–238.
25. Adolfson J. Human performance and behaviour in hyperbaric environments. Stockholm: Almquist & Wiksell, 1967.
26. Adolfson J. Berghage TE. Perception and performance underwater. New York: John Wiley & Sons, 1974.
27. Teichner WH. Comments. In: Bachrach AJ, ed. The development of standardized assessment of underwater performance. The fourth undersea medical society workshop. Report number WS:3-20-75. Bethesda: Undersea Medical Society, 1973:16–17.
28. Shilling CW, Werts MF, Schandelmeier NR, eds. The underwater handbook. A guide to physiology and performance for the engineer. New York: Plenum Press, 1977:386–400.
29. Steinberg H. Selective effects of an anaesthetic drug on cognitive behaviour. Q J Exp Psychol 1954; 6:170–180.
30. Kiessling RJ, Maag CH. Performance impairment as a function of nitrogen narcosis. J Appl Psychol 1962; 46:91–95.
31. Biersner RJ, Hall DA, Linaweaver PG, Neuman TS. Diving experience and emotional factors related to the psychomotor effects of nitrogen narcosis. Aviat Space Environ Med 1978; 49: 959–962.
32. Hesser CM, Fagraeus L, Adolfson J. Roles of nitrogen, oxygen, and carbon dioxide in compressed-air narcosis. Undersea Biomed Res 1978; 5:391–400.
33. Adam N. Effects of general anesthetics on memory functions in man. J Comp Physiol Psychol 1973; 83:294–305.
34. Himwich HE. Brain metabolism and cerebral disorders. Baltimore: Williams & Wilkins, 1951.
35. Baddeley AD. Diver performance. In: Woods JD, Lythgoe JN, eds. Underwater science. An introduction to experiments by divers. London: Oxford, 1971:33–67.
36. Frankenhaeuser M, Beckman M. The susceptibility of intellectual functions to a depressant drug. Scand J. Psychol 1961; 2:93–99.
37. Walsh JM, Thomas JR, Thorne DR, Bachrach AJ. Differential performance changes under hyperbaric conditions. Aerosp Med 1972; 43:623–625.
38. Reynolds GS. A primer of operant conditioning. Glenview, IL: Scott Foresman, 1968.
39. Thompson T, Grabowski JG. Reinforcement schedules and multioperant analysis. New York: Appleton Century Crofts, 1972.
40. Honig WK, Staddon JER. Handbook of operant behavior. Englewood Cliffs, NJ: Prentice Hall, 1977.
41. Jennings RD. Nitrogen narcosis and rat behavior on fixed-ratio and differential-reinforcement-of-low-rate schedules. J Comp Physiol Psychol 1973; 83:515–522.

42. Thomas JR, Walsh JM, Bachrach AJ, Thorne DR. Differential behavioral effects of nitrogen, helium, and neon at increased pressures. In: Lambertsen CJ, ed. Underwater physiology V. Proceedings of the fifth symposium on underwater physiology. Bethesda: Federation of American Societies for Experimental Biology, 1976:641–649.
43. Thomas JR. Nitrogen, helium and neon effects on timing behavior at increased pressures. Aerosp Med 1973; 44:45–48.
44. Thomas JR, Bachrach AJ. Modification of operant performance in pigeons by increased pressures of nitrogen and helium. Undersea Biomed Res 1974; 1:181–188.
45. Jennings RD, Breck B. Rat operant responding: An indicator of nitrogen narcosis? Aviat Space Environ Med 1975; 46:922–929.
46. Thomas JR. Changes in progressive-ratio performance under increased pressures of air. J Exp Anal Behav 1974; 21:553–562.
47. Fowler B, Granger S. A theory of inert gas narcosis effects on performance. In: Bachrach AJ, Matzen MM, eds. Underwater physiology VII. Proceedings of the seventh symposium on underwater physiology. Bethesda: Undersea Medical Society, 1981:403–413.
48. Hamilton K, Fowler B, Porlier G. Interaction of inert gas narcosis with alcohol and amphetamine. Undersea Biomed Res 1984; 11 (Suppl): 22.
49. Welford AT. Fundamentals of skill. London: Methuen, 1968.
50. Berry C, Gelder MG, Summerfield A. Experimental analysis of drug effects on human performance using information theory concepts. Br J Psychol 1965; 56:255–265.
51. Baddeley AD. Selective attention and performance in dangerous environments. Br J Psychol 1972; 63:537–546.
52. Bartus RT. Impairments in primate information processing resulting from nitrogen narcosis. Physiol Behav 1974; 12:797–804.
53. Shiffrin RM. Capacity limitations in information processing, attention and memory. In: Estes WK, ed. Handbook of learning and cognitive processes. Vol 4. Attention and memory. Hillsdale, NJ: Lawrence Erlbaum, 1976:177–236.
54. Sanders AF. Structural and functional aspects of the reaction process. In: Dornic S, ed. Attention and performance VI. Proceedings of the sixth international symposium on attention and performance. Hillsdale, NJ: Lawrence Erlbaum, 1977:3–25.
55. Craik FIM, Levy BA. The concept of primary memory. In: Estes WK, ed. Handbook of learning and cognitive process. Vol 4. Attention and memory. Hillsdale NJ: Lawrence Erlbaum, 1976:133–175.
56. Näätänen R. The inverted-U relationship between activation and performance: A critical review. In: Kornblum S, ed. Attention and performance IV. New York: Academic Press, 1973:155–174.
57. Thayer RE. Toward a psychological theory of multidimensional activation (arousal). Motiv Emotion 1978; 2:1–34.
58. Vanderwolf CH, Robinson TE. Reticulo-cortical activity and behavior: A critique of the arousal theory and a new synthesis. Behav Brain Sci 1981; 4:459–514.
59. Hockey R, Hamilton P. The cognitive patterning of stress states. In: Hockey GRJ, ed. Stress and fatigue in human performance. Chichester: John Wiley & Sons, 1983:331–362.
60. Pachella RG. The interpretation of reaction time in information-processing research. In: Kantowitz BH, ed. Human information processing: Tutorials in performance and cognition. Hillsdale, NJ: Lawrence Erlbaum, 1974:41–82.
61. Rabbit PMA. Sequential reactions. In: Holding D, ed. Human skills. Chichester: John Wiley & Sons, 1981:153–175.
62. Sanders AF. Stage analysis of reaction processes. In: Stelmach GE, Requin J, eds. Tutorials in motor behavior. Amsterdam: Elsevier North-Holland, 1980: 331–354.
63. Posner MI, McLeod P. Information processing models—in search of elementary operations. Ann Rev Psychol 1982; 33:477–514.
64. NcNicol D. A primer of signal detection theory. London: George Allen & Unwin, 1972.
65. Banks WW, Berghage TE, Heaney DM. Visual recognition thresholds in a compressed air environment. Aviat Space Environ Med 1979; 50:1003–1006.
66. Adam N, Collins GI. Search in short-term memory during inhalation of a general anesthetic in man. T.-I.-T. Life Sci 1977; 7:53–58.

67. Adolfson J. Deterioration of mental and motor functions in hyperbaric air. Scand J Psychol 1965; 6:26–32.
68. Bradley ME, Dickson JG. The effect of nitrous oxide narcosis on the physiologic and psychologic performance of man at rest and during exercise. In: Lambertsen CJ, ed. Underwater physiology V. Proceedings of the fifth symposium on underwater physiology. Bethesda: Federation of American Societies for Experimental Biology, 1976:617–626.
69. Davey CP. Physical exertion and mental performance. In: Welford AT, ed. Man under stress. London: Taylor & Francis, 1974:29–33.
70. Fuster JM. Effects of stimulation of brain stem on tachistoscopic perception. Science 1958; 127:150–153.
71. Goodman SJ. Visuo-motor reaction times and brain stem multiple-unit activity. Exp Neurol 1968; 22:367–378.
72. Goodman SJ, Mann PEG. Reticular and thalamic multiple unit activity during wakefulness, sleep and anesthesia. Exp Neurol 1967; 19:11–24.
73. Webb AC. Consciousness and the cerebral cortex. Br J Anaesth 1983; 55:209–219.
74. Fowler B, White PL, Holness DE, Wright GR, Ackles KN. The effects of inert gas narcosis on the speed and accuracy of movement. Ergonomics 1982; 25:203–212.
75. Steinberg H, Legge D, Summerfield A. Drug-induced changes in visual perception. In: Rothlin E, ed. Neuropharmacology. Vol 2. Proceedings of the second meeting of the collegium internationale neuro-psychopharmacologicum. Amsterdam: Elsevier, 1961:392–396.
76. Fluur E, Adolfson J. Hearing in hyperbaric air. Aerosp Med 1966; 37:783–785.
77. Adolfson J, Fluur E. Hearing discrimination in hyperbaric air. Aerosp Med 1967; 38:174–175.
78. Thomas JR. Auditory discrimination under increased pressures of helium-oxygen and air. Psychol Rep 1973; 32:159–164.
79. Legge D. Analysis of visual and proprioceptive components of motor skill by means of a drug. Br J Psychol 1965; 56:243–254.
80. Adolfson JA, Goldberg L, Berghage TE. Effects of increased ambient air pressures on standing steadiness in man. Aerosp Med 1972; 43:520–524.
81. Carter RC, Mewha MK, Lash LE. Nitrous oxide and tremor. US Navy Experimental Diving Unit. Navxdivingu Report 10-75. Panama City, FL, 1975.
82. Chapman CR, Murphy TM, Butler SH. Analgesic strength of 33 percent nitrous oxide: A signal detection theory analysis. Science 1973; 179:1246–1248.
83. Frankenhaeuser M. Estimation of time. Stockholm: Almquist & Wiksell, 1959:103–111.
84. Adam N, Rosner BS, Hosick EC, Clark DL. Effect of anesthetic drugs on time production and alpha rhythm. Percept Psychophys 1971; 10:133–135.
85. Adam N, Castro AD, Clark DL. Production estimation and reproduction of time intervals during inhalation of a general anesthetic in man. J Exp Psychol 1974; 102:609–614.
86. Shilling CW, Willgrube WW. Quantitative study of mental and neuromuscular reactions as influenced by increased air pressure. US Navy Med Bull 1937; 35:373–380.
87. Craik FIM. Encoding and retrieval effects in human memory: A partial review. In: Long L, Baddeley A, eds. Attention and performance IX. Hillsdale, NJ: Lawrence Erlbaum, 1981: 383–401.
88. Baddeley AD. Working memory. Philos Trans R Soc Lond 1983; B302:311–324.
89. Hitch GJ. Developing the concept of working memory. In: Claxton G, ed. Cognitive psychology: New directions. London: Routledge & Kegan Paul, 1980:154–196.
90 Fowler B. Effect of hyperbaric air on short-term and long-term memory. Aerosp Med 1973; 44:1017–1022.
91. Frankenhaeuser M. Effects of nitrous oxide on subjective and objective variables. Scand J Psychol 1963; 4:37–43.
92. Fowler B, Ackles KN. Effect of hyperbaric air on long-term memory organization and recall. Aviat Space Environ Med 1975; 46:655–659.
93. Hamilton K, Fowler B, Taylor M, Porlier G. The effects of inert gas narcosis on memory functioning. Paper presented at the annual scientific meeting of the Great Lakes Chapter of the Undersea Medical Society. Toronto, September, 1982.
94. Hamilton K, Fowler B, Porlier G. Amelioration of narcotic memory deficits: Practical and theoretical implications. Paper presented at the Great Lakes Chapter of the Undersea Medical Society. Buffalo, October, 1983.

95. Eysenck MW. Arousal, learning and memory. Psychol Bull 1976; 83:389–404.
96. Berry C. Effects of a drug and immediate memory. Nature 1965; 207:1012.
97. Berry C. Individual differences in short-term memory. Nature 1968; 220:302–303.
98. Summerfield A. Drugs and human behavior. Br Med Bull 1964; 20:70–74.
99. Whitaker LA, Findley MS. Nitrogen narcosis measured by dual task performance. J Appl Psychol 1977; 62:735–746.
100. US Navy Diving Manual. Air diving. Vol I. Carson, CA: Best, 1979:3–20.
101. Eysenck MW. Anxiety and individual differences. In: Hockey GRJ, ed. Stress and fatigue in human performance. Chichester: John Wiley & Sons, 1983:273–298.
102. Biersner RJ, Edwards D, Bailey LW. Effects of nitrous oxide on responses of divers to personality tests. Percept Mot Skills 1974; 38:1091–1097.
103. Edmonds C, Lowry C, Pennefather J. Diving and subaquatic medicine. Mosman, NSW: Diving Medical Centre, revised 2nd ed. Chap 9, 1983.
104. Freitag M, Woods A. Commercial diving reference and operations handbook. Chichester: John Wiley & Sons, 1983:193–194.
105. Zinkowksi NB. Commercial oil-field diving. Second ed. Cambridge: Cornell Maritime Press, 1978:18–19.
106. Walsh JM, Bachrach AJ. Adaptation to nitrogen narcosis manifested by timing behavior in the rat. J Comp Physiol Psychol 1974; 86:883–889.
107. Moeller G, Chattin CP. Situation-specific experience and nitrogen narcosis in the diving environment. J Appl Psychol 1975; 60:154–158.
108. Baddeley AD. Influence of depth on the manual dexterity of free divers: A comparison between open sea and pressure chamber testing. J Appl Psychol 1966; 50:81–85.
109. Moeller G, Chattin C, Rogers W, Laxar K, Ryack B. Performance effects with repeated exposure to the diving environment. J Appl Psychol 1981; 66:502–510.
110. Muren A, Adolfson J, Örnhagen H, Gennser M, Hamilton RW. Nisahex: Deep nitrox saturation with nitrox and trimix excursions. In: Bachrach AJ, Matzen MM, eds. Underwater physiology VIII. Bethesda: Federation of American Societies for Experimental Biology, 1984:713–729.
111. Warburton DM. Brain, behaviour and drugs. London: John Wiley & Sons, 1975:136–158.
112. Synodinos NE. Selective impairment by nitrogen narcosis of performance on a digit-copying and a mental task. Ergonomics 1976; 19:69–80.
113. Elcombe DD, Teeter JH. Nitrogen narcosis during a 14-day continuous exposure to 5.2% O_2 in N_2 at pressure equivalent to 100 fsw (4 ATA). Aerosp Med 1973; 44:864–869.
114. McKay CL, Strauss MS, Kinney JAS, Luria SM. Visual evoked responses, EEG's, and reaction time during a normoxic saturation dive, NISAT I. Undersea Biomed Res 1977; 4: 131–145.
115. Bennett PB, Poulton EC, Carpenter A, Catton MJ. Efficiency at sorting cards in air and a 20 percent oxygen-helium mixture at depths down to 100 feet and in enriched air. Ergonomics 1967; 10:53–62.
116. Bean JW. Tensional changes of alveolar gas in reactions to rapid compression and decompression and question of nitrogen narcosis. Am J Physiol 1950; 161:417–425.
117. Rashbass C. The unimportance of carbon dioxide in nitrogen narcosis. Medical Research Council. Royal Naval Personnel Research Committee. Underwater Physiological Sub-Committee Report No 163. Alverstoke, Hants. October, 1955.
118. Case EM, Haldane JBS. Human physiology under high pressure. J Hyg 1941; 41:225–249.
119. Frankenhaeuser M, Graff-Lonnevig V, Hesser CM. Effects on psychomotor functions of different nitrogen-oxygen mixtures at increased ambient pressures. Acta Physiol Scand 1963; 59:400–409.
120. Thomas JR. Combined effects of elevated pressures of nitrogen and oxygen on operant performance. Undersea Biomed Res 1974; 1:363–370.
121. Thomas JR, Burch LS, Banvard RA. Interaction of hyperbaric nitrogen and oxygen effects on behavior. Aviat Space Environ Med 1976; 47:965–968.
122. Hesser CM, Adolfson J, Fagraeus L. Role of CO_2 in compressed air narcosis. Aerosp Med 1971; 42:163–168.
123. Adolfson J, Fagraeus L, Hesser CM. Deterioration of standing steadiness in hyperbaric environment. Forsvarsmedicin 1973; 9:253–256.

124. Braithwaite WR, Berghage TE, Crothers JC. Postural equilibrium and vestibular response at 49.5 ATA. Undersea Biomed Res 1974; 1:309–323.
125. Morrison JB, Reimers SD. Design principles of underwater breathing apparatus. In: Bennett PB, Elliott DH, eds. The physiology and medicine of diving. Third ed. London: Baillière, Tindall, 1982:55–98.
126. Frankenhaeuser M, Graff-Lonnevig V, Hesser CM. Psychomotor performance in man as affected by high oxygen pressure (3 atmospheres). Acta Physiol Scand 1960; 50:1–7.
127. Ackerman MJ, Spencer JW. Brain stimulation in rats exposed to hyperbaric environments. Undersea Biomed Res 1976; 3:369–378.
128. Bennett PB. Review of protective pharmacological agents in diving. Aerosp Med 1972; 43: 184–192.
129. Berkowitz BA, Finck AD, Ngai SH. Nitrous oxide analgesia: Reversal by naloxone and development of tolerance. J Pharmacol Exp Ther 1977; 203: 539–547.
130. Fink AD, Ngai SH, Berkowitz BA. Antagonism of general anesthesia by naloxone in the rat. Anesthesiology 1977; 46:241–245.
131. Harper MH, Winter PM, Johnson BH, Eger EI. Naloxone does not antagonize general anesthesia in the rat. Anesthesiology 1978; 49:3–5.
132. Bennett PB. Naloxone fails to antagonize the right response in rats anesthetized with halothane. Anesthesiology 1978; 49:9–11.
133. Nicodemus HF, McElroy H. Failure of naloxone or physostigmine to reverse nitrogen anesthesia in guinea pigs. Undersea Biomed Res 1981; 8:171–174.
134. Bennett PB, Leventhal BL, Coggin R, Roby J, Racanska L. Lithium effects: protection against nitrogen narcosis, potentiation of HPNS. Undersea Biomed Res 1980; 7:11–16.
135. Walsh JM, Burch LS. Reduction of the behavioral effects of Δ^9-tetrahydrocannabinol by hyperbaric pressure. Pharmacol Biochem Behav 1977; 7:111–116.
136. Frizza J, Chesher GB, Jackson DM, Malor R, Stormer GA. The effect of Δ^9-tetrahydrocannabinol, cannabidiol and cannabinol on the anaesthesia induced by various anaesthetic agents in mice. Psychopharmacology 1977; 55:103–107.
137. Wesnes K, Warburton DM. Stress and drugs. Hockey GRJ, ed. Stress and fatigue in human performance. Chichester: John Wiley & Sons, 1983:203–243.
138. Grossman SP, Sclafani A. Sympathomimetic amines. Furchtgott E, ed. Pharmacological and biophysical agents and behavior. New York: Academic Press, 1971:269–344.
139. Thomas JR, Walsh JM. Behavioral evaluation of pharmacological agents in hyperbaric air and helium oxygen. In: Shilling CW, Beckett MW, eds. Underwater physiology VI. Proceedings of the sixth symposium on underwater physiology. Bethesda: Federation of American Societies for Experimental Biology, 1978:69–77.
140. Alkana RL, Malcolm RD. Hyperbaric ethanol antagonism in mice: Studies on oxygen, nitrogen, strain, and sex. Psychopharmacology 1982; 77:11–16.
141. Jones AW, Jennings RD, Adolfson J, Hesser CM. Combined effects of ethanol and hyperbaric air on body sway and heart rate in man. Undersea Biomed Res 1979; 6:15–25.
142. Thomas JR. Amphetamine and chlordiazepoxide effects on behavior under increased pressures of nitrogen. Pharmacol Biochem Behav 1973; 1:421–426.
143. Walsh JM. Amphetamine effects on timing behavior in rats under hyperbaric conditions. Aerosp Med 1974; 45:721–726.
144. Thomas JR. Interaction between hyperbaric air and d-amphetamine effects on performance. Psychopharmacology 1976; 48:69–73.
145. Russell RL, Pihl RO. The effect of dose, novelty, and exploration on amphetamine-produced stereotyped behavior. Psychopharmacology 1978; 60:93–100.
146. Miller KW. Inert gas narcosis, the high pressure neurological syndrome, and the critical volume hypothesis. Science 1974; 185:184–186.
147. Brauer RW, Hogan PM, Hugon M, Macdonald AG, Miller KW. Patterns of interaction of effects of light metabolically inert gases with those of hydrostatic pressure as such—a review. Undersea Biomed Res 1982; 9:353–396.
148. Gruenau SP, Ackerman MJ. Quantification of high pressure nervous syndrome (HPNS) tremor in the guinea pig. Undersea Biomed Res 1978; 5:95–104.
149. Gruenau SP, Ackerman MJ. Tremor power spectra in guinea pigs: effect of intermediate holding pressure. Undersea Biomed Res 1978; 5:335–340.

150. Thomas JR. Reversal of nitrogen narcosis in rats by helium pressure. Undersea Biomed Res 1976; 3:249–259.
151. Baddeley AD, Flemming NC. The efficiency of divers breathing oxy-helium. Ergonomics 1967; 10:311–319.
152. Baddeley AD, de Figueredo JW, Hawkswell-Curtis JW, Williams AN. Nitrogen narcosis and performance underwater. Ergonomics 1968; 11:157–164.
153. Davis FM, Osborne JP, Baddeley AD, Graham IMF. Diver performance: nitrogen narcosis and anxiety. Aerosp Med 1972; 43:1079–1082.
154. Mears JD, Cleary PJ. Anxiety as a factor in underwater performance. Ergonomics 1980; 23: 549–557.
155. Baddeley A, Idzikowski C. Anxiety, manual dexterity and diver performance. Ergonomics 1985; 28: (in press).
156. Miller JW, ed. NOAA diving manual. Diving for science and technology. Second ed. Washington DC: US Government Printing Office, 1979:2-20–2-23.
157. Bennett PB. Inert gas narcosis and the high pressure nervous syndrome. In: Davis JC, ed. Hyperbaric and undersea medicine. San Antonio TX: Medical Seminars Inc., 1981:Vol 1, Lesson No 16.
158. Larn R, Whistler R. Commercial diving manual. Newton Abbot: David & Charles, 1984: 3.14.